ISSN 1070-3632, Russian Journal of General Chemistry, 2014, Vol. 84, No. 8, pp. 1496–1499. © Pleiades Publishing, Ltd., 2014.
Original Russian Text © T.P. Efimova, O.Yu. Ozerova, T.A. Novikova, R.I. Baichurin, V.M. Berestovitskaya, 2014, published in Zhurnal Obshchei Khimii, 2014, Vol. 84, No. 8, pp. 1268–1272.

Reactions of 1-Amino-2-nitroguanidine with 2-Aryl(hetaryl)-1-nitro-1-ethoxycarbonyl(benzoyl)ethenes

T. P. Efimova, O. Yu. Ozerova, T. A. Novikova, R. I. Baichurin, and V. M. Berestovitskaya

Herzen State Pedagogical University of Russia, nab. reki Moiki 48, St. Petersburg, 191186 Russia
e-mail: kohrgpu@yandex.ru

Received March 17, 2014

Abstract—Reactions of 1-amino-2-nitroguanidine with 2-aryl(hetaryl)-1-nitro-1-ethoxycarbonyl(benzoyl)-ethenes proceed via initial formation the aza-Michael product, are accompanied by liberation of nitroacetic ester (or nitroacetophenone), and result in *N*-aryl(hetaryl)methylidene-*N*-(2-nitroguanidino)amines.

Keywords: nitroguanidine, *gem*-alkoxycarbonyl(benzoyl)nitroethene, *N*-aryl(hetaryl)methylidene-*N*-(2-nitroguanidino)amine

DOI: 10.1134/S1070363214080088

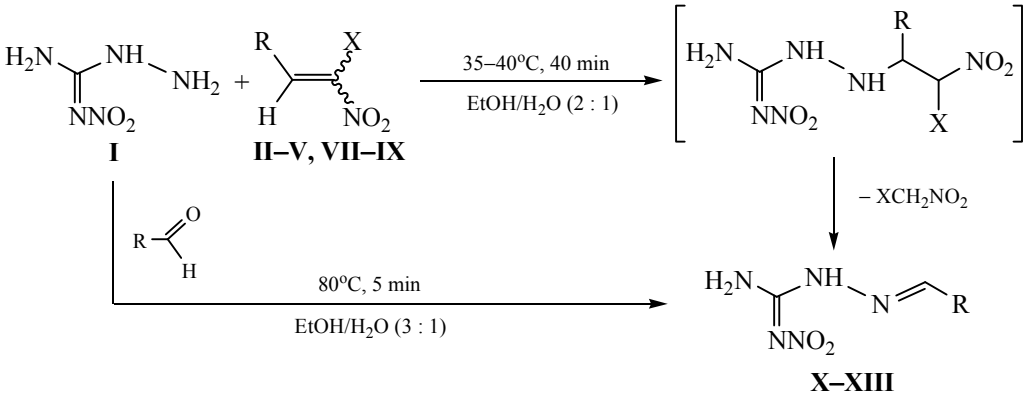
1-Amino-2-nitroguanidine is of particular interest as a synthon for synthesis of valuable biologically active and energy-rich compounds. In particular, some guanidine-containing compounds are used as drugs possessing hypotensive (clonidine, guanfacine, apraclonidine, and guanabenz) and hypoglycemic (phenformin, metformin, and buformin) activities [1–3].

Certain nitroguanidine derivatives have found agriculture application. For instance, patent [4] describes method for *N*-arylmethylidene-*N*-(2-nitroguanidino)-amines preparation and the products use as insecticides.

Previously, we studied the reaction of 2-aryl-1-nitro- and 1-bromo-1-nitroethenes with 1-amino-2-nitroguanidine, yielding the amination products: 1-nitro- and 2-aryl-1-bromo-1-nitro-2-(2-nitroguanidino-amino)ethanes [5]. In the presence of basic catalyst or upon prolonged refluxing the adducts derived from *gem*-bromonitrostyrenes were cleaved to form *N*-arylmethylidene-*N*-(2-nitroguanidino)amines.

Extending our studies in that area, herein we report the reactions of 1-amino-2-nitroguanidine **I** with *gem*-ethoxycarbonyl- and *gem*-benzoylnitroethenes. 1-Amino-2-nitroguanidine **I** reacted with 2-aryl(hetaryl)-1-nitro-1-ethoxycarbonylethenes **II–V** in aqueous-alcoholic medium at 35–40°C within 40 min to yield high-melting crystalline *N*-aryl(hetaryl)methylidene-*N*-

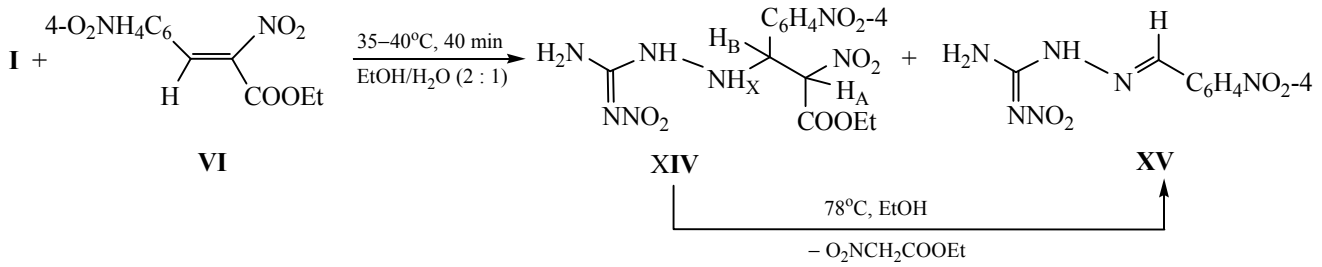
Scheme 1.



I **II–V, VII–IX** **X–XIII**

X = $COOC_2H_5$, R = C_6H_5 (**II**), 4-$CH_3OC_6H_4$ (**III**), 2-thienyl (**IV**), 2-furyl (**V**); X = COC_6H_5, R = C_6H_5 (**VII**), 2-thienyl (**VIII**), 2-furyl (**IX**); R = C_6H_5 (**X**), 4-$CH_3OC_6H_4$ (**XI**), 2-thienyl (**XII**), 2-furyl (**XIII**).

Scheme 2.



(2-nitroguanidino)amines **X**–**XIII** with yields of up to 90% (Scheme 1).

Apparently, the reactions proceeded via the initial formation of the adducts followed by elimination of nitroacetic ester. The elimination readiness depended significantly on the nature of the substituent in the aromatic ring: the electron-donating substituents were expected to promote that process, and the electron-withdrawing groups should have inhibited it. Indeed, 1-nitro-2-(4-nitrophenyl)-1-ethoxycarbonylethene **VI** (containing the electron-withdrawing nitro group in *para*-position of the aromatic ring) yielded a mixture of the adduct XIV and the elimination product **XV** in the 1 : 1 ratio (1H NMR) in the reaction with the similar conditions (^{1}H NMR). Attempts to separate that mixture were not successful: recrystallization from ethanol resulted in azomethine **XV** (Scheme 2).

Reactions of 1-amino-2-nitroguanidine with *gem*-benzoylnitroethenes **VII**–**IX** as well as with their ester analogs proceeded via the Ad_N–E mechanism, i.e., they were accompanied by nitroacetophenone elimination and yielded the corresponding *N*-aryl(hetaryl)methylidene-*N*-(2-nitroguanidino)amines **X**, **XII**, and **XIII**.

Obviously, the driving force of the transformation of the initially formed adducts into azomethines was elimination of the resonance-stabilized anions of nitroacetic ester (or nitroacetophenone) along with favorable energetics of the final conjugated products.

Physical characteristics of the obtained aryl(hetaryl) methylideneguanidinoamines **XI**–**XIII** coincided with those of model compounds prepared by authentic synthesis from the corresponding aromatic aldehydes and 1-amino-2-nitroguanidine; the mixing test did not reveal any melting point depression.

Structures of the obtained compounds were confirmed by ^{1}H NMR, IR, and electronic absorption spectroscopy. The spectral data of **X** and **XV** coincided with those of the same compounds synthesized independently [5].

Signals of the protons of all the structural fragments were identified in ^{1}H NMR spectra of compounds **XI**–**XIII**. Protons of the =CH, NH_2, and NH groups resonated in the weak field at 8.05–8.30, 8.11–8.76, 8.11–8.76, and 11.69–11.81 ppm, respectively. The signals at 6.62–7.83 ppm were assigned to protons of the aromatic and heterocyclic rings. IR spectra of compounds **XI**–**XIII** contained sets of strong absorption bands. Absorption bands of the N–H bonds stretching were observed in the high-frequency part of the spectra (3206–3222, 3343–3363, and 3438–3477 cm^{-1}). Absorption bands at 1612–1633 cm^{-1} could be probably attributed to stretching of the C=N bond and to deformation of the N–H bond. Absorbance at 1426–1440 and 1313–1338 cm^{-1} was assigned to the NNO_2 group stretching. IR spectral features of compounds **XI**–**XIII** were in line with those of the structurally similar compounds prepared previously [5, 6].

Strong absorption bands at λ_{max} of 328–337 nm (ε = 28000–33000 L mol^{-1} cm^{-1}) observed in electronic absorption spectra of **XI**–**XIII** were characteristic of chromophore system of such compounds [5, 7].

^{1}H NMR spectrum of a mixture of **XIV** and **XV** contained the proton signals of the both compounds. The doublet signals at 6.06–7.79 ppm, characteristic of the H_B, NH_X, H_A multispin system of two diastereomers **a** and **b** (in the ratio of 3.4 : 1), were assigned to the adduct **XIV**. Broadened proton signals of the primary (7.58 and 8.54 ppm) and secondary (9.32 and 9.37 ppm) amino groups of nitroguanidine fragments of the two diastereomers were found in the weak-field part of the spectrum. The protons of =CH, NH_2, and NH groups of **XV** resonated at 8.19, 8.91–8.94, and 4.12 ppm, respectively.

EXPERIMENTAL

^{1}H NMR spectra were recorded with the Jeol ECX400A spectrometer (DMSO-d_6, 399.78 MHz; residual solvent protons as internal reference). IR spectra were registered with the Shimadzu IRPrestige-

21 Fourier-spectrometer (KBr). Electronic spectra were recorded with the Shimadzu UV-2401 PC spectrophotometer (ethanol, quartz cell, l = 0.1 cm, $c \approx$ 0.3 mmol/L). Elemental analysis was performed with the EuroVector EA 3000 analyzer (CHN Dual mode).

1-Amino-2-nitroguanidine **I** was prepared as described elsewhere [8].

gem-Ethoxycarbonylnitroethenes **II**, **III** [9], **IV**, and **V** [10]; *gem*-benzoylnitroethenes **VII** [11], **VIII,** and **IX** [12] were prepared via condensation of aldehydes with ethyl nitroacetate [13] or nitroacetophenone [14] upon heating in benzene in the presence of acetic acid and β-alanine in a flask equipped with the Dean–Stark trap. 1-Nitro-2-(4-nitrophenyl)-1-ethoxy-carbonylethene **VI** was synthesized via condensation of nitroacetic ester with *N*-(4-nitro-phenylmethylidene)-*n*-butylamine [15].

***N*-Benzylidene-*N*-(2-nitroguanidino)amine (X).** *a*. A solution of 0.27 g (2.2 mmol) of 1-amino-2-nitroguanidine **I** in 10 mL of water was added to a solution of 0.55 g (2.2 mmol) of 1-nitro-2-phenyl-1-ethoxycarbonylethene **II** in 20 mL of ethanol. The reaction mixture was stirred at 40°C during 40 min and then cooled to 18–20°C. The precipitated crystals were filtered off, washed sequentially with water, ethanol, and diethyl ether, and dried in air. Yield 0.36 g (80%), mp 182–183°C (ethanol–water, 2 : 1) (mp 182–185°C [5]). Found, %: C 47.05; H 4.50; N 34.17. $C_8H_9N_5O_2$. Calculated, %: C 46.37; H 4.34; N 33.81.

b. A solution of 0.27 g (2.2 mmol) of 1-amino-2-nitroguanidine **I** in 10 mL of water was added a solution of 0.52 g (2.2 mmol) of 1-benzoyl-1-nitro-2-phenylethene **VII** in 20 mL of ethanol. The reaction mixture was stirred at 40°C during 40 min and then cooled to 18–20°C. The precipitated crystals were filtered off, washed sequentially with water, ethanol, and diethyl ether, and dried in air. Yield 0.38 g (85%), mp 183–184°C (ethanol–water, 2 : 1). The mixing test with the sample obtained via the method *a* did not reveal any depression of the melting point.

***N*-(4-Methoxyphenylmethylidene)-*N*-(2-nitroguanidino)amine (XI).** *a*. Prepared similarly to compound **X**, method *a* from 0.4 g (1.6 mmol) of 2-(4-methoxyphenyl)-1-nitro-1-ethoxycarbonylethene **III** and 0.19 g (1.6 mmol) of 1-amino-2-nitroguanidine **I**. Yield 0.35 g (92%), mp 201–203°C (ethanol–water, 2 : 1). IR spectrum, ν, cm^{-1}: 1313, 1426 (NNO_2), 1619, 1633 (C=N), 3206, 3363, 3477 (NH). ^{1}H NMR spectrum, δ, ppm: 6.95 d and 7.77 d (4H, 4-$CH_3OC_6H_4$, J 8.8 Hz), 8.06 s (1H, =CH), 8.43 s and 8.74 s (2H, NH_2), 11.69 s (1H, NH). Electronic absorption spectrum, λ_{max}, nm (ε): 332 (33000). Found, %: C 45.56; H 29.53; N 4.64. $C_9H_{11}N_5O_3$. Calculated, %: C 46.14; H 29.73; N 4.70.

b. A solution of 0.17 g (1.5 mmol) of 1-amino-2-nitroguanidine **I** in 10 mL of water was added to a solution of 0.2 g (1.5 mmol) of 4-methoxybenzaldehyde in 10 mL of ethanol. The mixture was stirred at 80°C during 5 min and then cooled down. The precipitated crystals were filtered off. Yield 0.33 g, mp 202–203°C (ethanol–water, 2 : 1). The mixing test with the sample obtained via the method *a* did not reveal any depression of the melting point.

***N*-(2-Nitroguanidino)-*N*-(2-thienylmethylidene)-amine (XII).** *a*. Prepared similarly to compound **X**, method *a* from 0.32 g (1.4 mmol) of 1-nitro-2-(2-thienyl)-1-ethoxycarbonylethene **IV** and 0.17 g (1.4 mmol) of 1-amino-2-nitroguanidine **I**. Yield 0.23 g (73%), mp 189–192°C (ethanol–water, 2 : 1). IR spectrum, ν, cm^{-1}: 1338, 1440 ($N–NO_2$), 1620, 1635 (C=N), 3222, 3343, 3438 (NH). ^{1}H NMR spectrum, δ, ppm: 7.10 d.d (1H, C_4H_3S, J 5.0, J 3.6 Hz), 7.49 d.d (1H, C_4H_3S, J 3.6, J 1.1 Hz), 7.69 d.d (1H, C_4H_3S, J 5.0, J 1.1 Hz), 8.30 s (1H, =CH), 8.11 s and 8.76 s (2H, NH_2), 11.81 s (1H, NH). Electronic absorption spectrum, λ_{max}, nm (ε): 337 (28000). Found, %: C 33.80; H 32.85; N 3.31. $C_6H_7N_5O_2S$. Calculated, %: C 34.00; H 32.11; N 2.94.

b. Prepared similarly to compound **X**, method *b* from 0.34 g (1.5 mmol) of 1-benzoyl-1-nitro-2-(2-thienyl)ethene **VIII** and 0.17 g (1.5 mmol) of 1-amino-2-nitroguanidine **I**. Yield 0.25 g (78%), mp 189–191°C (ethanol–water, 2 : 1).

c. Prepared similarly to compound **XI**, method *b* from 0.16 g (1.5 mmol) of thiophene-2-carbaldehyde and 0.17 g (1.5 mmol) of 1-amino-2-nitroguanidine **I**. Yield 0.30 g (95%), mp 190–192°C (ethanol–water, 2 : 1). The mixing test did not reveal any depression of the melting point.

***N*-(2-Nitroguanidino)-*N*-(2-furylmethylidene)-amine (XIII)**. *a*. Prepared similarly to compound **X**, method *a* from 0.29 g (1.4 mmol) of 1-nitro-2-(2-furyl)-1-ethoxycarbonylethene **V** and 0.167 g (1.4 mmol) of 1-amino-2-nitroguanidine **I**. Yield 0.22 g (81%), mp 203–205°C (ethanol–water, 2 : 1). IR spectrum, ν, cm^{-1}: 1328, 1430 ($N–NO_2$), 1612, 1622 (C=N), 3218, 3345, 3443 (NH). ^{1}H NMR spectrum, δ,

ppm: 6.62 d.d (1H, C_4H_3O, *J* 1.7, *J* 3.4 Hz), 7.03 d (1H, C_4H_3O, *J* 3.4 Hz), 7.83 d (*J* 1.7 Hz), 8.05 s (1H, =CH), 8.22 s and 8.75 s (2H, NH_2), 11.79 s (1H, NH). Electronic absorption spectrum, λ_{max}, nm (ε): 328 (29600). Found, %: C 36.54; H 3.55. $C_6H_7N_5O_3$. Calculated, %: C 37.03; H 3.61.

b. Prepared similarly to compound **X,** method *b* from 0.36 g (1.5 mmol) of 1-benzoyl-1-nitro-2-(2-furyl)ethene **IX** and 0.17 g (1.5 mmol) of 1-amino-2-nitroguanidine **I**. Yield 0.23 g (78%), mp 204–205°C (ethanol–water, 2 : 1).

c. Prepared similarly to compound **XI,** method *b* from 0.14 g (1.5 mmol) of furfural and 0.17 g (1.5 mmol) of 1-amino-2-nitroguanidine **I**. Yield 0.28 g (95%), mp 203–205°C (ethanol–water, 2 : 1). The mixing test did not reveal any depression of the melting point.

Ethyl 2-nitro-3-(2-nitroguanidinoamino)-3-(4-nitrophenyl)propanoate (XIV) and *N*-(2-nitroguanidino)-*N*-(4-nitrophenylmethylidene)amine (XV). A solution of 0.12 g of 1-amino-2-nitroguanidine **I** in 10 mL of water was added to a solution of 0.26 g of 1-nitro-2-(4-nitrophenyl)-1-ethoxycarbonylethene **VI** in 20 mL of ethanol. The reaction mixture was stirred at 40°C during 30 min and then cooled to 18–20°C. The precipitated crystals were filtered off, washed sequentially with water, ethanol, and diethyl ether, and dried in air to yield 0.16 g of a mixture of **XIV** and **XV** in the ratio of 1 : 1 (^{1}H NMR). After recrystallization from ethanol, only compound **XV** was isolated, mp 241–243°C (ethanol–water, 2 : 1) (mp 240–242°C [5]). Found N, %: 32.57. $C_8H_8N_6O_4$. Calculated N, %: 33.33.

ACKNOWLEDGMENTS

Physico-chemical studies were performed in the Center for Collective Use in Herzen State Pedagogical University of Russia.

This work was financially supported by the Ministry of Education of Russia in the frame of the basic part of the governmental task.

REFERENCES

1. Mashkovskii, M.D., *Lekarstvennye sredstva* (Drugs), Moscow: RIA "Novaya Volna," 2012.
2. Granik, V.G., *Osnovy meditsinskoi khimii* (Fundamentals of Medicinal Chemistry), Moscow: Vuzovskaya Kniga, 2001, p. 291.
3. Granik, V.G. *Lekarstva (farmakologicheskii, biologicheskii i khimicheskii aspekty)* [Drugs (Pharmacological, Biological and Chemical Aspects)], Moscow: Vuzovskaya Kniga, 2006, p. 209.
4. Zhaohai, Q., China Patent 2216324 A1, 2010.
5. Efimova, T.P., Ozerova, O.Yu., Belik, I.V., Novikova, T.A., and Berestovitskaya, V.M., *Rus. J. Gen. Chem*., 2012, vol. 82, no. 8, p. 1409. DOI: 10.1134/S1070363212080129
6. Morozova, N.S., Metelkina, E.L., Novikova, T.A., Shlyapochnikov, V.A., Sergienko, O.I., and Perekalin, V.V., *Zh. Org. Khim*., 1983, vol. 19, no. 6, p. 1228.
7. Novikova, T.A., Metelkina, E.L., Efimova, T.P., Zaskokina, D.V., and Berestovitskaya, V.M., *Russ. J. Org. Chem*., 2005, vol. 41, no. 6, p. 938. DOI: 10.1007/s11178-005-0271-2.
8. Henry, R.A., Makovsky, R.C., and Smith, G.B.L., *J. Am. Chem. Soc*., 1951, vol. 73, no. 1, p. 474. DOI: 10.1021/ja01145a513.
9. Baichurin, R.I., Baichurina, L.V., Aboskalova, N.I., and Berestovitskaya, V.M., *Russ. J. Gen. Chem*., 2013, vol. 83, no. 9, p. 1764. DOI: 10.1134/S1070363213090223.
10. Baichurina, L.V., Baichurin, R.I., Aboskalova, N.I. and Berestovitskaya, V.M., *Russ. J. Gen. Chem*., 2010, vol. 80, no. 10, p. 2022. DOI: 10.1134/S1070363210100221.
11. Sokolov, N.A., Tishchenko, I.G., Karpitskaya, N.V., and Grinkevich, V.G., *Vestn. BGU*, 1978, Ser. 2, no. 3, p. 29.
12. Berestovitskaya, V.M., Aboskalova, N.I., Ishmaeva, E.A., Bakhareva, S.V., Berkova, G.A., Vereshchagina, Ya.A., Fel'gendler, A.V., and Fattakhova, G.R., *Russ. J. Gen. Chem*., 2001, vol. 71, no. 12, p. 1942. DOI: 10.1023/A:1014200612456.
13. *Sintezy organicheskikh soedinenii* (Synthesis of Organic Compounds), Eds A.N. Nesmeyanov, P.A. Bobrov, Moscow: Izd. Akad. Nauk SSSR, 1950, no. 1, p. 117.
14. Long, L.M. and Troutman, H.D., *J. Am. Chem. Soc*., 1949, vol. 71, no. 7, p. 2469. DOI: 10.1021/ja01175a067.
15. Dornow, A. and Menzel, H., *Lieb. Ann*., 1954, vol. 588, no. 1, p. 40. DOI: 10.1002/jlac.19545880105.